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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,514	12/18/2001	Philip J. Barr	368292000200	6421
25213	7590	02/02/2005	EXAMINER	
HELLER EHRMAN WHITE & MCAULIFFE LLP 275 MIDDLEFIELD ROAD MENLO PARK, CA 94025-3506			WALICKA, MALGORZATA A	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 02/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/025,514

Applicant(s)

BARR ET AL.

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 October 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-10 and 12-41 is/are pending in the application.
- 4a) Of the above claim(s) 3,5-7,9,10,12-15,18-35 and 38-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2 and 8 is/are rejected.
- 7) ☒ Claim(s) 4, 16, 17, 36, and 37 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Amendment in Response to Non-final Office Action filed Oct. 29, 2004 is acknowledged. Claims 2 and 30 are amended. Claims 2-10 and 12-41 are pending. Claims 3, 5-7, 9, 10, 12-15, 18-35 and 38-41 are withdrawn from examiner's consideration as drawn to non-elected invention. Claims 2, 4, 8, 16, 17 and 36-37 are under examination.

Detailed Office Action

1. Request for rejoinder

Applicants emphasized their request for rejoinder of method claims 26-35 and 38-41. As indicated in previous Office Actions, the issue will be addressed when allowable composition claims are identified.

2. Rejection under 35 U.S.C 103

Claim 2 and 8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over the same prior art, which was used in the rejection of July 22, 2004 i.e., Australian document AU-B-13288/88 with priority date March 20, 1987 as applied to claim 2 above, and further in view of the article by Bingle L. et al., Thorax, Dec. 1996, vol. 51/12, pages 1273-1274.

The claims are directed to a fusion protein comprising alpha 1-antitrypsin or a functionally active portion thereof, and secretory leukocyte protease inhibitor or a functionally active portion thereof, wherein said fusion protein has alpha 1-antitrypsin activity and secretory leukocyte protease inhibitor activity.

The Australian document teaches construction of hybrid serpins: "Besides the possibility of producing hybrid serpins having altered substrate specificity or activity, the invention **provides an approach to the preparation of bifunctional proteins**, which, for example, contain the activities of angiotensin II and antitrypsin", page 5, line 21. Thus, the Australian document teaches productions of hybrid serpin that possesses two active centers, i.e. the hybrid that consists of at least active fragments of alpha 1-antitrypsin and angiotensin. However, the Australian document does not teach the fusion protein consisting of alpha 1-antitrypsin and secretory leukocyte inhibitor activity.

Bingle et al. strongly suggest that secretory leukocyte protease inhibitor and alpha 1-protease inhibitor, i.e. alpha 1-antitrypsin, are the most effective for treatment of such diseases as inflammatory lung disorders such as emphysema, bronchiectasis, pulmonary fibrosis, acute lung injury and bronchopulmonary dysplasia **when used in combination**; see page 1274, the text bridging the left and right column.

It would have been obvious to one having ordinary skill in the art at the time of invention to have a hybrid serpin as taught by the Australian document and modify it so that it contained the secretory leukocyte protease inhibitor and alpha 1-antitrypsin or their active fragments. The expectation of success was very high because the Australian document teaches that a fusion protein containing at least active fragments of alpha 1-antitrypsin and other serpin, acts as a bifunctional serpin. The motivation to combine alpha 1-antitrypsin and human secretory leukocyte inhibitor in one fusion protein was provided by Bingle et al., because they teach that combination of both activities is of high therapeutic importance, which is the greater that the SLPI was

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shown to possess anti-HIV activity at physiological concentrations. Therefore combining both serpins would provide therapeutics of large range of action, fighting lung disorders including those related to HIV. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Traversing rejection under this section Applicants, in their Remarks of October 29, 2004 Applicants argue, that the language of Bingle's speculative review does not provide strong motivation for use of both alpha 1-antitrypsin and SLPI; "falls somewhat short of 'strongly suggest[ing]' the coadministration of the two protease inhibitors", page 9, line 16. Furthermore, in Applicants' opinion Bingle's suggestion that both serpins should be coadministered, would not have motivated the fusion of the active agents. Finally, Applicants conclude Bingle teaches away from the invention.

Applicants' arguments have been fully considered but are found unpersuasive for the following reasons. It is common in the art that ideas presented in review articles are reduced to practice by those skilled in the art. As to the strength of Binble's suggestion, the title is self-evident: "Secretory leukoprotease inhibitor: partnering alpha 1-proteinase inhibitor to combat pulmonary inflammation [emphasis added] ". Partnering means to associate as a partner, which in the disputable case of use of two proteins does not exclude their fusion.

Furthermore, Applicants indicate that the examiner misread the Australian patent and took human leuserpin 1 (hLS2) as LSPI. Applicants pinpoint, "this is not the SLPI/AAT fusion of applicants'claims 2 and 8." Although this is true, because, the

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rejection for obviousness does not require that prior art teaches all the limitations of the claimed invention and provides 100% expectation of success, Applicants' arguments do not preclude the use of the patent as prior art in rejection under 35 USC, section 103, in its above version.

5. Conclusion

As stated in the previous Office Actions, the claims contain allowable subject matter. Claims 4, 16, 17, 36 and 37 are objected to as depending on rejected claim 2 but would be allowable if rewritten in an independent form.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.

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Patent Examiner


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